

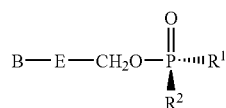
TABLE 7-continued

| Excretion and Tissue Distribution of Radiolabelled GS-7340 in Dogs (Mean, N = 2) Following an Oral Dose at 10 mg-eq. PMPA/kg. | | | | | |
|--|---------|--------------------|---------|--------------------|--------------------------------|
| Tissue/Fluid | GS-4331 | | GS-7340 | | Ratio of GS 7340 to GS-4331 |
| | % Dose | Conc. (ug-eq/g) | % Dose | Conc. (ug-eq/g) | |
| Bile | 0.00 | 9.63 | 0.22 | 40.48 | 4.2 |
| Feces | 40.96 | n.d. | 0.19 | n.d. | n.a. |
| Total GI Tract Contents | 5.61 | n.d. | 21.64 | n.d. | n.a. |
| Urine | 23.72 | n.d. | 14.73 | n.d. | n.a. |
| Plasma at 24 h | 0.00 | 0.20 | 0.00 | 0.20 | 1.0 |
| Plasma at 0.25 h | n.a. | 3.68 | n.a. | 3.48 | 0.9 |
| PBMC* | 0.00 | n.d. | 0.00 | 63.20 | n.d. |
| Whole Blood | 0.00 | 0.85 | 0.16 | 0.20 | 0.2 |
| Total Recovery | 81.10 | | 68.96 | | |

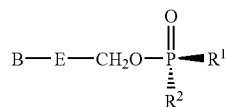
Calculated using typical recovery of 15×10^6 cells total, and mean PBMC volume of 0.2 picoliters/cell
 n.s. = no sample,
 n.a. = not applicable,
 n.d. = not determined.

The invention claimed is:

1. A diastereomerically enriched compound having the structure (3)



which contains less than 40% by weight of the diastereomer (4)



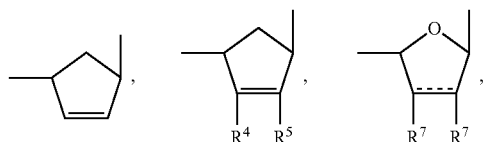
wherein

R¹ is an oxyester which is hydrolyzable in vivo, or hydroxyl;

B is a heterocyclic base;

R² is hydroxyl, or the residue of an amino acid bonded to the P atom through an amino group of the amino acid and having each carboxy substituent of the amino acid optionally esterified, but not both of R¹ and R² are hydroxyl;

E is $-(\text{CH}_2)_2-$, $-\text{CH}(\text{CH}_3)\text{CH}_2-$, $-\text{CH}(\text{CH}_2\text{F})\text{CH}_2-$, $-\text{CH}(\text{CH}_2\text{OH})\text{CH}_2-$, $-\text{CH}(\text{CH}=\text{CH}_2)\text{CH}_2-$, $-\text{CH}(\text{C}=\text{CH})\text{CH}_2-$, $-\text{CH}(\text{CH}_2\text{N}_3)\text{CH}_2-$,



$-\text{CH}(\text{R}^6)\text{OCH}(\text{R}^6)-$, $-\text{CH}(\text{R}^9)\text{CH}_2\text{O}-$ or $-\text{CH}(\text{R}^8)\text{O}-$, wherein the right hand bond is linked to the heterocyclic base;

the broken line represents an optional double bond;

R⁴ and R⁵ are independently hydrogen, hydroxy, halo, amino or a substituent having 1-5 carbon atoms selected from acyloxy, alkoxy, alkylthio, alkylamino and dialkylamino;

R⁶ and R^{6'} are independently H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl, or C₂-C₇ alkanoyl;

R⁷ is independently H, C₁-C₆ alkyl, or are taken together to form $-\text{O}-$ or $-\text{CH}_2-$;

R⁸ is H, C₁-C₆ alkyl, C₁-C₆ hydroxyalkyl or C₁-C₆ haloalkyl; and

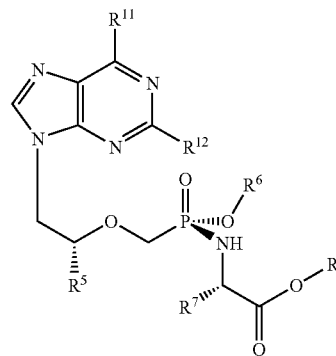
R⁹ is H, hydroxymethyl or acyloxymethyl;

and their salts, free base, and solvates.

2. The compound of claim 1 containing less than 20% by weight of the diastereomer (4).

3. The compound of claim 1 containing less than 5% by weight of the diastereomer (4).

4. A diastereomerically enriched compound having the structure (5a)



which contains less than 40% by weight of diastereomer (5b)

